The physiological role of leptin for anthropometrical changes in pregnancy

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INTRODUCTION

Leptin is a hormone consisting of 167 amino acids. Its production and secretion are controlled by the obesity gene [1]. By its structure, leptin belongs to the first class cytokines [2].

The main source of the leptin synthesis is a fat tissue [3–5]. It can be synthesized in small amounts by stomach mucous membrane, breast glandular tissue cells, myocytes and in the case of pregnancy by placenta tissue as well [1, 6–8]. There are some suggestions that the brain produces leptin as well [9].

In the blood, leptin circulates free or with binding proteins [10, 11]. It was also thought that proteins binding leptin can be soluble forms of leptin receptors. This is a common feature of most combinations belonging to the cytokine family [12].

Leptin concentration in the blood directly depends on BMI and especially on fat tissue amount. The synthesis and secretion of the hormone fluctuate on a daily basis (circadian rhythm) [13, 14].

Leptin is acting through specific receptors located in the brain, lungs, kidneys, liver, ovaries, the...
stem haematopoietic cells, placenta tissue, etc. [15]. Leptin is a kind of signal for the central nervous system providing it with the possibility to regulate the amount of fat in the body and to utilize the energy received [16]. The hypothalamus is an important part of the brain where leptin compressively affects the neuropeptide Y (NPY) that stimulates hunger. Leptin modifies the nutrition habits and has an effect on the biosynthesis of most neurotransmitters that are suppressing the appetite [17, 18]. It has been also determined that leptin stimulates the sympathetic nervous system [19].

The physiological role of leptin in pregnancy is still mysterious. Pregnancy can be treated as a hypermetabolic condition - within the period of pregnancy the body weight and fat tissues are growing very quickly, and various neuroendocrinial processes keep the energy balance positive.

The concentration of leptin in the blood serum of pregnant women is higher as compared to that of non-pregnant women [20]. Almost all authors state that the longer the pregnancy period, the larger leptin amounts can be found in the woman’s body; the largest leptin amount is found in the third trimester of pregnancy and later these indices remain unchanged up to the end of the pregnancy [21–23].

The concentration of leptin in the blood serum of a woman in the later period of pregnancy is three times that compared to the earlier pregnancy period [24, 25].

It is suggested that the physiological role of leptin in the female body in the period of pregnancy is aimed at foetal development and growth [26, 27].

Taking into consideration the suggestion that the role of leptin in the period of pregnancy is not limited to the regulation of the foetal growth, investigations showed that leptin to affect the hemopoiesis and angiogenesis in different development stages [28].

Leptin production is regulated by steroid hormones, and this has been confirmed by lots of research [29]. It has been concluded that estrogens stimulate transcription in the tissues that produce leptin.

It was expected that leptin as a regulator of foetal and placental development could be connected to the processes that are common in lactation and neonatal growth. It has been proven that leptin concentration in the bodies of breast-feeding women is considerably higher compared to that of non-feeding women [30].

The literature data show that leptin takes part in most of the physiological processes in the human of bodyk. Leptin concentration indices fluctuate increase in the later stage of pregnancy when the female’s anthropometrical indices and metabolism have been changed.

Therefore, changes in female anthropometrical indices and leptin concentration and their interrelations can be treated as the criteria of normal physiological pregnancy development.

The goal of this study was to examine leptin concentration in maternal blood serum and its relationship to maternal anthropometry.

MATERIALS AND METHODS

A group of 67 women was examined in the Outpatient Department of Vilnius Maternity Hospital in 2001–2005, of them 30 were examined only once, during the period of delivery. Only women with a normal course of pregnancy, without any complications and pathology were selected. The age of the women ranged from 18 to 39 years. The average age was 26.8 years (95% CI 25.8–27.7).

More than 90% of all women fell into the 21–35-year age range. The current pregnancy was the first for 43 women (44.3%), 55.7% women having had pregnancies in the past; some had abortions, and therefore real primiparas came to a little more than half of the sample – 57 (58.8%). Primiparas were a little younger than non-primiparas, the average age being 24.8 and 29.6 years, respectively.

They were examined three times during the period of pregnancy - in 7–13, 14–26 and 27–40 weeks of gestation. During each visit they were examined anthropometrically and blood samples were taken from vein for leptin analysis. Anthropometrical examination included the following parameters: height, weight, body mass index, thickness of skin folds, sizes of body (abdominal, chest, hip, waist and arm).

Skin folds were measured with a calliper: in total, ten skin folds were analysed (submental, pectoral, subscapular, anterior of arm (bicipital), posterior of arm (tricipital), abdominal, suprailiac, femoral, knee, calf. Using three folds (tricipital, suprailiac, femoral) representing three parts of the body, body density and the percentage of body fat were calculated according to Siri formula [31] as the most commonly used. Relative and absolute amount of body fat was also assessed by the bioelectric impedance method with Omron BF 302 equipment (Omron Matsusaka Co Ltd., Japan) [32].

Leptin levels were assessed by the radioimmune method [33] with IMMUNOTECH equipment (Praha, Czech Republic). Statistical analysis was performed using Microsoft Excel 2000 software. For various parameters (averages, percentage), 95 percent confidence intervals were calculated. Statistical significance of differences between continuous variables was evaluated using Student’s criteria. Differences were considered significant at the reliability level p < 0.05.

Approval for the study was obtained from the Ethics Committee at each participating centre and all patients gave their informed consent after oral and written information.
The physiological role of leptin for anthropometrical changes in pregnancy

73

RESULTS

The height of the women ranged from 154 to 184 cm, mean 167.7 cm (95% CI 166.5–168.8 cm).

The weight of the women before pregnancy ranged from 47 to 97.5 kg, mean 62.2 kg (95% CI 60.1–64.4 kg).

The average BMI value was 22.10 kg/m² (95% CI 21.43–22.7). Most women (up to 80% of the total sample) had normal BMI ranging within 18.5–22.49 kg/m² (normal range for that age group according to WHO standards).

The primiparas had a slightly lower BMI than women with second pregnancy – 21.51 and 22.95, respectively (statistically significant, p = 0.049).

Women gained weight up to 15.4 kg on average (range, 10 to 18 kg). The average weight in the end of pregnancy was 77.1 kg (95% CI 74.6–79.6). It showed that the absolute weight gain (in kg) did not depend upon woman’s weight before pregnancy.

The size of hip, thigh and arm increases due to increment of subcutaneous fat and are related to the passive body mass. Only the increment of arm circumference was not statistically significant (p > 0.05). More abundant increment of fat was observed in the lower part of the body – the lower part of the trunk and legs (the female type of bodily constitution becomes more apparent).

Correlation analysis of body sizes was performed for different periods (trimesters) of pregnancy (Fig. 1).

All correlation coefficients are statistically significant to a very high level (p < 0.01); the correlation matrix is not presented in the summary. Both dendrograms (trimesters I and III) are very similar by the agglomeration schedule of measurements. The five parameters distribute into two clusters. One is formed by the abdominal and chest sizes; however, at the end of pregnancy their interrelation is not as close as at the beginning, because different factors influence their increment. Hip, thigh and arm sizes form the next cluster. These parameters remain closely related till the end of pregnancy, because all of them are related to the increasing amount of subcutaneous fat.

Data on the dynamics of skin fold thickness are presented in Table 1.

A specially marked increment was found for subscapular, submental, suprailliac and thigh

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<thead>
<tr>
<th>Skin folds</th>
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<th>2nd half</th>
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<td>M ± m</td>
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<tr>
<td>Sub mental</td>
<td>8.82 ± 0.44</td>
<td>4.0–16.2</td>
<td>10.13 ± 0.45</td>
<td>5.0–17.4</td>
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<tr>
<td>Pectoral</td>
<td>11.29 ± 0.75</td>
<td>4.0–22.0</td>
<td>12.15 ± 0.77</td>
<td>5.0–24.0</td>
<td>0.19</td>
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<tr>
<td>Sub scapular</td>
<td>14.02 ± 0.90</td>
<td>6.2–30.2</td>
<td>16.09 ± 0.88</td>
<td>8.0–30.0</td>
<td>0.00002</td>
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<tr>
<td>Bicipital</td>
<td>7.77 ± 0.59</td>
<td>2.2–24.2</td>
<td>9.35 ± 0.69</td>
<td>2.0–21.2</td>
<td>0.0012</td>
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<td>Tricipital</td>
<td>14.04 ± 0.77</td>
<td>6.2–29.0</td>
<td>12.77 ± 0.65</td>
<td>5.8–24.0</td>
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<td>Abdominal</td>
<td>17.89 ± 0.77</td>
<td>6.7–28.0</td>
<td>16.60 ± 0.74</td>
<td>6.0–26.7</td>
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<tr>
<td>Suprailliac</td>
<td>17.91 ± 0.89</td>
<td>6.2–33.0</td>
<td>19.96 ± 0.80</td>
<td>11.0–32.2</td>
<td>0.00099</td>
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<tr>
<td>Thigh</td>
<td>24.32 ± 0.75</td>
<td>14.2–34.8</td>
<td>27.32 ± 0.88</td>
<td>15.8–38.0</td>
<td>0.0003</td>
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<tr>
<td>Knee</td>
<td>9.31 ± 0.51</td>
<td>5.0–19.0</td>
<td>10.58 ± 0.69</td>
<td>4.4–25.2</td>
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<td>Sural</td>
<td>13.85 ± 0.58</td>
<td>5.0–22.0</td>
<td>15.89 ± 0.73</td>
<td>9.0–28.0</td>
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* – thickness decreased.

Fig. 1. Cluster analysis dendrogram of correlation matrix of body sizes (A – first half of pregnancy, B – second half of pregnancy): 1 – abdominal, 2 – chest; 3 – hip, 4 – thigh, 5 – arm

Fig. 2. Cluster analysis dendrogram of correlation matrix of skin fold (A – first half, B – second half of pregnancy). Skin folds: 1 – sub mental, 2 – pectoral, 3 – sub scapular, 4 – anterior of arm (bicipital), 5 – posterior of arm (tricipital), 6 – abdominal, 7 – suprailliac, 8 – thigh, 9 – knee, 10 – calf
skin folds. It means that more adipose tissue is added on the trunk and on the proximal part of legs. Other skin folds located on both limbs (arm, knee, calf) increased not so markedly, and the tricipital skin fold even decreased.

The correlation analysis of skin fold thickness was performed for different periods (trimesters) of pregnancy (the correlation matrices are not presented in this summary; all the coefficients are statistically significant). Cluster analysis of correlation matrices of skin folds was performed. The results are presented as dendrograms in Fig. 2.

During the first half of pregnancy (Fig. 1, A) all skin folds are distributed into two main clusters. The first cluster combines skin folds mostly located on the trunk (except anterior skin fold of the arm, and the second cluster combines skin folds of the lower limb and a tricipital skin fold. It means that in spite of a comparatively even distribution of subcutaneous adipose tissue there could be slight differences between trunk and limbs. In the second half of pregnancy the dendrogram (Fig. 2, B) revealed a closer correlation between the skin folds of trunk and limbs (in general, the agglomeration schedule is similar), except the folds of thighs and abdomen, which stand out from the main cluster.

In the subsequent analysis it is better not to use separate skin folds but rather their sum.

It is notable that there is a marked difference between trimesters I and II; during trimester III this increment is not so significant.

Two methods were used for estimation of passive body mass: the bioelectric impedance method and the calculation of body fat according to skin fold thickness.

These two methods gave us different results. The significant changes of body fat revealed by the bioelectric impedance method show a more (p < 0.001) significant increase of the relative and absolute values of total body fat, the differences reaching 6% and 5 kg, respectively. The calculated body fat is of a lower value (the average absolute difference is 2.6 kg). The difference can be explained by the fact that calculating the amount of fat (according to skin fold thickness) we get subcutaneous fat, whereas the bioelectric impedance method reveals also visceral adipose fat (maybe also the body fat of the foetus).

Changes of serum leptin level are presented in Table 2.

At the end of pregnancy (during delivery) leptin level was lower than during trimester I, its average value being 22.23 ± 3.25 ng/ml.

To elucidate the correlation between the anthropometrical parameters and leptin level, analysis of the correlation matrices were performed, and the results are presented in Table 3.

Leptin strongly correlated with weight (p < 0.01), body sizes (p < 0.005) and the average sum of nine skin folds (p < 0.01) both a the beginning and end of pregnancy.

**DISCUSSION**

Worldwide, more and more studies are carried out with the aim to measure and evaluate the influence of various factors affecting the anthropometrical alterations and physiological changes in pregnancy [34, 35]. For the first time in Lithuania we have analyzed anthropometrical parameters, especially with respect to the recently discovered hormone leptin.

Many authors state that leptin concentration in maternal circulation is increasing within the later stages of pregnancy. The highest leptin concentration was detected in the third pregnancy trimester, and it remained high up to the end of labour [21–23]. In our research, the highest leptin concentration was detected within the second pregnancy trimester, and these levels were completely different as compared to the analogous levels of the first pregnancy trimester. Within the third trimester of pregnancy we detected a lower leptin concentration in the blood serum compared to the second pregnancy trimester, however, these levels were much

<table>
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<th>Table 2. Changes of leptin level during pregnancy trimesters</th>
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<td>Trimesters</td>
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<td>Trimester I (n = 33)</td>
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<td>Trimester II (n = 34)</td>
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<td>Trimester III (n = 45)</td>
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<th>Table 3. Correlation between leptin level and anthropometrical parameters in the first and second half of pregnancy</th>
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<td>Height</td>
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<td>Arm size</td>
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<td>Sum of skin folds</td>
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* p < 0.05; ** p < 0.001.
higher than in the first pregnancy trimester, while blood serum leptin concentration in was considerably decreased during delivery. Therefore, it is possible that delivery factors (such as stress, physical activity, i.e. birth pangs) suppress leptin production [14].

Our research showed an obvious correlation between leptin concentration in maternal circulation during the first and the second trimesters of pregnancy and the anthropometrical parameters (summarized indices related to body mass, body dimensions and fat folds). These results are identical to data presented by other authors who also state that blood serum leptin concentration in directly depends on female BMI prior to pregnancy and especially on the amounts of fat tissues [10, 11].

It is possible to suppose that the role of leptin during pregnancy is related to fast foetal growth, considering that in our research the highest concentration of leptin in maternal circulation was detected within the second trimester of pregnancy. This statement was verified by the correlation established between leptin concentration in maternal circulation and summarized indices of fat folds. Also, the increase in serum leptin level during pregnancy might attribute to the transfer of placental leptin to maternal circulation.

Results of the current research have shown that the most considerable changes in anthropometrical parameters during pregnancy occur in passive body mass connected to fat accumulation in the lower body part of pregnant women. Hormonal changes during pregnancy have a significant effect on fat tissue metabolism. Fat tissue, pear-shape accumulation in the lower body part can be treated as an important phenomenon of pregnancy related to hyperestremia and hyperleptinemia. Pear-shape type fat tissue accumulation is also connected to the fast lipolysis at the end of pregnancy and preparation for lactation.

This means that the anthropometrical parameters of pregnant women are conditioned by the metabolic activity of the leptin hormone.

CONCLUSIONS

Our study showed that during pregnancy leptin manifested itself in the feminine type of body composition: adipose tissue accumulated mostly in the regions of hips and thighs. The anthropometry of women was significantly associated with leptin. These associations are necessary for modification of maternal homeostasis to provide nutritional support for the developing foetus and preparation for lactation following delivery.

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References

FIZIOLOGINIS LEPTINO VAIDMUO
ANTROPOMETRINIAMS POKYĖIAMS NĖDŽTUMO METU

Santrauka
Hormonas leptinas dalyvauja daugelyje fiziologiniø procesø. Manoma, kad pagrindinis leptino vaidmuo yra reguliuoti energijos sunaudojimà bei kûno riebalø kiekû. Nëdžtumas – tai fiziologinë moters bûklë, kai per trumpà laikà sparëiai auga nëdžtumo svoris, vyksta naujø audiniø sintezë bei hormoniniai pokyèiai. Nëdžtumo hiperleptinemija susijusi su nãèõtumo pradþio svorio, kûno apimkoèio, kraujo serumo leptino koncentracijos didëjimu nuo nãèãtumo pradþio iki III nãèãtumo trimestro (nuo 26,8 ± 2,0 ng/ml iki 34,1 ± 2,0 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Hiperleptinemija taip pat buvo nustatyta ir III nãèãtumo trimestrà (28,3 ± 3,2 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trimestrà (37,1 ± 2,3 ng/ml). Didãðiausia leptino koncentracija buvo nustatyta II nãèãtumo trim...